

The retinoids bind to one or more retinoic acid receptors to initiate diverse processes such as reproduction, development, bone formation, cellular proliferation and differentiation, apoptosis, hematopoiesis, immune function and vision. Retinoids are required to maintain normal differentiation and proliferation of almost all cells and have been shown to reverse/suppress carcinogenesis in a variety of in vitro and in vivo experimental models of cancer, see (Moon et al., Ch. 14 Retinoids and cancer. In *The Retinoids*, Vol. 2. Academic Press, Inc. 1984). Also see Roberts et al. Cellular biology and biochemistry of the retinoids. In *The Retinoids*, Vol. 2. Academic Press, Inc. 1984, hereby incorporated by reference), which also shows that vesanoid (tretinoid trans retinoic acid) is indicated for induction of remission in patients with acute promyelocytic leukemia (APL).

A synthetic description of retinoid compounds, hereby incorporated by reference, is described in: Dawson MI and Hobbs PD. The synthetic chemistry of retinoids: in *The retinoids*, 2<sup>nd</sup> edition. MB Sporn, AB Roberts, and DS Goodman(eds). New York: Raven Press, 1994, pp 5-178.

Lingen et al. describe the use of retinoic acid and interferon alpha against head and neck squamous cell carcinoma (Lingen, MW et al., Retinoic acid and interferon alpha act synergistically as antiangiogenic and antitumor agents against human head and neck squamous cell carcinoma. *Cancer Research* 58 (23) 5551-5558 (1998), hereby incorporated by reference).

Iurlaro et al. describe the use of beta interferon and 13-cis retinoic acid to inhibit angiogenesis.

(Iurlaro, M et al., Beta interferon inhibits HIV-1 Tat-induced angiogenesis: synergism with 13-cis retinoic acid. European Journal of Cancer 34 (4) 570-576 (1998), hereby incorporated by reference).

- 5       Majewski et al. describe Vitamin D3 and retinoids in the inhibition of tumor cell-induced angiogenesis. (Majewski, S et al., Vitamin D3 is a potent inhibitor of tumor cell-induced angiogenesis. J. Invest. Dermatology. Symposium Proceedings, 1 (1), 97-101 (1996), hereby  
10       incorporated by reference.

- Majewski et al. describe the role of retinoids and other factors in tumor angiogenesis. Majewski, S et al., Role of cytokines, retinoids and other factors in tumor angiogenesis. Central-European journal of Immunology 21  
15       (4) 281-289 (1996), hereby incorporated by reference).

- Bollag describes retinoids and alpha-interferon in the prevention and treatment of neoplastic disease. (Bollag W. Retinoids and alpha-interferon in the prevention and treatment of preneoplastic and neoplastic  
20       diseases. Chemotherapie Journal, (Suppl) 5 (10) 55-64 (1996), hereby incorporated by reference.

- Bigg, HF et al. describe all-trans retinoic acid with basic fibroblast growth factor and epidermal growth factor to stimulate tissue inhibitor of  
25       metalloproteinases from fibroblasts. (Bigg, HF et al., All-trans-retinoic acid interacts synergistically with basic fibroblast growth factor and epidermal growth factor to stimulate the production of tissue inhibitor of metalloproteinases from fibroblasts. Arch. Biochem.  
30       Biophys. 319 (1) 74-83 (1995), hereby incorporated by reference).

Nonlimiting examples of retinoids that may be used in the present invention are identified in Table No. 13 below.

5 Table No. 13. Retinoids

Compound	Common Name/ Trade Name	Company	Reference	Dosage
CD-271	Adapaline		EP 199636	
Tretinoin trans retinoic acid	Vesanoid	Roche Holdings		45 mg/M <sup>2</sup> /day as two evenly divided doses until complete remission
2,4,6,8- Nonatetraen oic acid, 9-(4- methoxy- 2,3,6- trimethylph enyl)-3,7- dimethyl- , ethyl ester, (all-E)-	etretinate isoetret- in; Ro-10- 9359; Ro- 13-7652; Tegison; Tigason	Roche Holdings	US 4215215	.25 - 1.5 mg/kg/day
Retinoic acid, 13-	isotret- inoin	Roche Holdings	US 4843096	.5 to 2 mg/kg/day